

Amendments to the Claims:

Please cancel claims 5 and 16 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in a future continuation or divisional application.

Please amend claims 1, 3-4, 6-9, 11-15, 17-18, 20-28, 31-36, and add new claims 39-63 as set forth below.

1. (Currently amended) A method for treating a disease or disorder with an underlying dysregulation of the emotional functionality comprising administering to a patient ~~the use of~~ a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, ~~and~~ wherein said compound is administered to said a patient in a dose ranging between 5 and 15 mg of the active ingredient.

2. (Original) The method of claim 1 wherein said compound is PIPAMPERONE.

3. (Currently amended) The method of claim 2, wherein said disease or disorder is selected from the group consisting of ~~comprising~~ anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

4. (Currently amended) The method of according to claim 1 or 2 wherein further comprising administering to the patient a second compound is administered simultaneously with, separate from or sequential to a the first compound as defined in claim 1 ~~or 2~~ to augment the therapeutic effect of said second compound or to provide a faster onset of the therapeutic effect of said second compound.

5. (Canceled)

6. (Currently amended) The method of claim 4, ~~or 5~~ wherein said second compound has a therapeutic effect on a disease or disorder is selected from the group consisting of comprising mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

7. (Currently amended) The method of claim 4, any of claims 4 to 6 wherein the first compound is administered daily at least one day before administering said second compound.

8. (Currently amended) The method of claim 4, wherein any of claims 4 to 7 said second compound is a selective serotonin re-uptake inhibitor.

9. (Currently amended) The method of claim 8, wherein said selective serotonin re-uptake inhibitor is chosen from the group consisting of ~~comprising~~ CITALOPRAM, fluoxetine, venlafaxine, fluvoxamine, paroxetine, sertraline, milnacipran and duloxetine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

10. (Original) The method of claim 9 wherein said serotonin re-uptake inhibitor is CITALOPRAM and is administered in a dose ranging between 10 and 40 mg of the active ingredient.

11. (Currently amended) A method for treating a disease or disorder with an underlying dysregulation of the emotional functionality comprising administering to a patient ~~the use of a composition comprising~~ a first compound having (i) a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT<sub>2A</sub> receptor with a pKi value equal to or higher than 8 towards the 5-HT<sub>2A</sub> receptor and less than 8 towards other 5HT receptors.

12. (Currently amended) The method of claim 11, wherein said disease or disorder is selected from the group consisting of ~~comprising~~ mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or

neglect.

13. (Currently amended) The method of claim 11, ~~or 12~~ wherein said first compound is chosen from the group consisting of ~~comprising~~ PIPAMPERONE, FANANSERIN, L-745,870, PNU-101387G and U-101387, and wherein said second compound is chosen from the group consisting of ~~comprising~~ PIPAMPERONE, FANANSERIN, ORG 5222, ZOTEPINE, OLANZEPINE, CLOZAPINE, S16924, S18327, AMPEROZIDE, SERTINDOLE, MDL 100.907, TIOSPIRONE, FLUSPIRILENE, OCAPERIDONE, RISPERIDONE and ZIPRASIDONE, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

14. (Currently amended) The method of claim 11, ~~any of claims 11 to 13~~ wherein said compounds are ~~composition is~~ administered to said a patient in a dose ranging between 0.5 µg and 300 mg for each of the active ingredients.

15. (Currently amended) The method of claim 11, ~~any of claims 11 to 14~~ wherein the first compound and the second compound are ~~said composition is~~ administered simultaneously with, separate from or sequential to a third compound to augment the therapeutic effect of said third compound or to provide a faster onset of the therapeutic effect of said third compound.

16. (Canceled)

17. (Currently amended) The method of claim 15, ~~or 16~~ wherein said third compound is a selective serotonin re-uptake inhibitor.

18. (Currently amended) The method of claim 17, wherein said selective

serotonin re-uptake inhibitor is chosen from the group consisting of ~~comprising~~ CITALOPRAM, fluoxetine, venlafaxine, fluvoxamine, paroxetine, sertraline, milnacipran and duloxetine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

19. (Original) The method of claim 18 wherein said serotonin re-uptake inhibitor is CITALOPRAM and is administered in a dose ranging between 10 and 40 mg of the active ingredient.

20. (Currently amended) A method for treating a disease or disorder ~~as defined in claim 12~~ with an underlying dysregulation of the emotional functionality comprising administering to a patient the use of a compound as defined in claim 1 or of a composition as defined in claim 11, characterized in that said compound or composition where the compound is administered simultaneously with, separate from or sequential to administering to said patient a nor-epinephrine re-uptake inhibitor to augment the therapeutic effect of said nor-epinephrine re-uptake inhibitor or to provide a faster onset of the therapeutic effect of said nor-epinephrine re-uptake inhibitor.

21. (Currently amended) A method for treating a disease or disorder ~~as defined in claim 12~~ with an underlying dysregulation of the emotional functionality comprising administering to a patient a first compound and a second compound the use of a compound as defined in claim 1 or of a composition as defined in claim 11, characterized in that where said compounds are or composition is administered simultaneously with, separate from or sequential to administering a nor-epinephrine re-uptake inhibitor to said patient to augment the therapeutic effect of said nor-epinephrine re-uptake inhibitor or to provide a faster onset of the therapeutic effect of said nor-epinephrine re-uptake inhibitor.

22. (Currently amended) The method according to claim 20, ~~or 24~~ wherein said nor-epinephrine re-uptake inhibitor is chosen from the group consisting of ~~comprising~~ tandamine, pirandamine, ciclazindol, fluparoxan, lortalamine, talsupram, talopram, prindamine, nomifensine, viloxazine, tomoxetine, duloxetine, venlafaxine, milnacipran and reboxetine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

23. (Currently amended) A method for treating a disease or disorder ~~as defined in claim 12~~ with an underlying dysregulation of the emotional functionality comprising administering to a patient the use of a compound as defined in claim 1 or of a composition as defined in claim 11, characterized in that said compound or composition where the compound is administered simultaneously with, separate from or sequential to administering to said patient a neuroleptic agent to augment the therapeutic effect of said neuroleptic agent or to provide a faster onset of the therapeutic effect of said neuroleptic agent.

24. (Currently amended) A method for treating a disease or disorder ~~as defined in claim 12~~ with an underlying dysregulation of the emotional functionality comprising administering to a patient a first compound and a second compound the use of a compound as defined in claim 1 or of a composition as defined in claim 11, characterized in that where said compounds are or composition is administered simultaneously with, separate from or sequential to administering a neuroleptic agent to said patient to augment the therapeutic effect of said neuroleptic agent or to provide a faster onset of the therapeutic effect of said neuroleptic agent.

25. (Currently amended) The method according to claim 23, ~~or 24~~ wherein said

neuroleptic agent is chosen from the group consisting of ~~comprising~~ chlorpromazine, haloperidol, perphenazine, thioridazine, mesoridazine, trifluoperazine, fluphenazine, clozapine, olanzapine, risperidone, ziprasidone, quetiapine, sertindole, aripiprazole, sonopiprazole, blonanserin, iloperidone, perospirone, raclopride, zotepine, DU-127090, ORG-5222, SM-13496, amisulpride, CP-361428, Lu 35-138, balaperidone, S-18327, WAY-135452, eplivanserin, E-5842, SR-31742, NE-100, osanetant, SR-141716, SR-48692, BSF-201640, BSF-190555, LAX-101a, sarizotan, CX-691 and SB-271046, or a pro-drug or active metabolite thereof, or a pharmaceutically acceptable salt thereof.

26. (Currently amended) A method for treating a disease or disorder ~~as defined in claim 12~~ with an underlying dysregulation of the emotional functionality comprising administering to a patient the use of a compound as defined in claim 1 or of a composition as defined in claim 11, characterised in that said compound or composition where the compound is administered simultaneously with, separate from or sequential to administering to said patient an NK1 antagonist to augment the therapeutic effect of said NK1 antagonist or to provide a faster onset of the therapeutic effect of said NK1 antagonist.

27. (Currently amended) A method for treating a disease or disorder ~~as defined in claim 12~~ with an underlying dysregulation of the emotional functionality comprising administering to a patient a first compound and a second compound the use of a compound as defined in claim 1 or of a composition as defined in claim 11, characterised in that where said compounds are or composition is administered simultaneously with, separate from or sequential to administering an NK1 antagonist to said patient to augment the therapeutic effect of said NK1 antagonist or to provide a faster onset of the therapeutic effect of said NK1 antagonist.

28. (Currently amended) The method according to claim 26, ~~or 27~~ wherein said NK1 antagonist is chosen from the group consisting of ~~comprising~~ MK-0869, GW597599, GW679769, GW823296, Compound A, NKP608, CP-96,345 (cis-3-(2-methoxybenzyl-amino-2-benzhydrylquinuclidine), CP-122721, CP-99994, GR-82334 (D-Pro9-[Spiro-y-lactam]-Leu10,Trp11)-Physalaemin(1-11)), R673, TAK-637, RPR100893 (perhydroisoindolol), RP-67580, LY303870, SR-140333 and trans-4-hydroxy-1-(1H-indol-3-ylcarbonyl)-L-prolyl-N-methyl-N-(phenylmethyl)-L-tyrosineamide (a derivative of FK888), or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

29. (Original) The method according to claim 28 wherein said NK1 antagonist is MK-0869 and is administered in a dose ranging between 10 and 160 mg of the active ingredient.

30. (Original) The method according to claim 29 wherein MK-0869 is administered in a dose of 80 mg of the active ingredient.

31. (Currently amended) The method according to claim 26, ~~any of claims 26 to 30~~ wherein the compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors serotonin re-uptake inhibitor is PIPAMPERONE.

32. (Currently amended) The method according to claim 31, ~~any of claims 26 to 30~~ wherein PIPAMPERONE is administered to the patient in a dose ranging between 5 and 15 mg of the active ingredient and wherein MK-0869 is administered to the patient in



a dose ranging between 10 and 160 mg of the active ingredient.

33. (Currently amended) A method for treating a musculoskeletal disease or disorder comprising administering to a patient the use of a compound as defined in claim 1 or of a composition as defined in claim 11, characterized in that said compound or composition where the compound is administered simultaneously with, separate from or sequential to administering to said patient a COX-2 inhibitor to augment the therapeutic effect of said COX-2 inhibitor or to provide a faster onset of the therapeutic effect of said COX-2 inhibitor.

34. (Currently amended) A method for treating a musculoskeletal disease or disorder comprising administering to a patient a first compound and a second compound the use of a compound as defined in claim 1 or of a composition as defined in claim 11, characterized in that where said compounds are or composition is administered simultaneously with, separate from or sequential to administering a COX-2 inhibitor to said patient to augment the therapeutic effect of said COX-2 inhibitor or to provide a faster onset of the therapeutic effect of said COX-2 inhibitor.

35. (Currently amended) The method of claim 33, ~~or 34~~ wherein said disease or disorder is selected from the group consisting of comprising rheumatoid arthritis, osteoarthritis and ~~or~~ ankylosing spondylitis.

36. (Currently amended) The method of claim 33, any of claims 33 to 35 wherein said COX-2 inhibitor is chosen from the group consisting of comprising celecoxib, rofecoxib, meloxicam, piroxicam, deracoxib, parecoxib, valdecoxib, etoricoxib, a chromene derivative, a chroman derivative, N-(2-cyclohexyloxynitrophenyl)methane sulfonamide, COX189, ABT963 and JTE-522, or a pro-drug or active metabolite thereof,

or a pharmaceutically acceptable salt thereof.

37. (Original) A method for preparing a compound having a selective D4 and 5-HT2A antagonist, reverse agonist or partial agonist activity comprising the following steps: (a) measuring the selective affinity of a test compound to the D4 receptor and selecting a compound that has a pKi value equal to or greater than 8 towards the D4 receptor in respect to all the other D receptors, and measuring the selective efficacy of the selected compound to the D4 receptor and selecting a compounds which is a selective antagonist, inverse agonist or partial agonist of the D4 receptor; (b) measuring the selective affinity of a test compound to the 5-HT2A receptor and selecting a compound that has a pKi value equal to or greater than 8 towards the 5-HT2A receptor in respect to all the other 5HT receptors, and measuring the selective efficacy of the selected compound to the 5-HT2A receptor and selecting a compounds which is a selective antagonist, inverse agonist or partial agonist of the 5-HT2A receptor; (c) identifying a compound which is selected in (a) and (b), (d) preparing the compound identified in (c).

38. (Original) Compound prepared by the method of claim 37.

39. (New) The method according to claim 21, wherein said nor-epinephrine re-uptake inhibitor is chosen from the group consisting of tandamine, pirandamine, ciclazindol, fluparoxan, lortalamine, talsupram, talopram, prindamine, nomifensine, viloxazine, tomoxetine, duloxetine, venlafaxine, milnacipran and reboxetine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

40. (New) The method of claim 20, wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other

psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

41. (New) The method of claim 21, wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

42. (New) The method according to claim 24, wherein said neuroleptic agent is chosen from the group consisting of chlorpromazine, haloperidol, perphenazine, thioridazine, mesoridazine, trifluoperazine, fluphenazine, clozapine, olanzapine, risperidone, ziprasidone, quetiapine, sertindole, aripiprazole, sonopiprazole, blonanserin, iloperidone, perospirone, raclopride, zotepine, DU-127090, ORG-5222, SM-13496, amisulpride, CP-361428, Lu 35-138, balaperidone, S-18327, WAY-135452, eplivanserin, E-5842, SR-31742, NE-100, osanetant, SR-141716, SR-48692, BSF-201640, BSF-190555, LAX-101a, sarizotan, CX-691 and SB-271046, or a pro-drug or active metabolite thereof, or a pharmaceutically acceptable salt thereof.

43. (New) The method of claim 23, wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

44. (New) The method of claim 24, wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

45. (New) The method according to claim 27, wherein said NK1 antagonist is chosen from the group consisting of MK-0869, GW597599, GW679769, GW823296, Compound A, NKP608, CP-96,345 (cis-3-(2-methoxybenzyl-amino-2-benzhydrylquinuclidine), CP-122721, CP-99994, GR-82334 (D-Pro9-[Spiro-y-lactam]-Leu10,Trp11)-Physalaemin(1-11)), R673, TAK-637, RPR100893 (perhydroisoindolol), RP-67580, LY303870, SR-140333 and trans-4-hydroxy-1-(1H-indol-3-ylcarbonyl)-L-

prolyl-N-methyl-N-(phenylmethyl)-L-tyrosineamide (a derivative of FK888), or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

46. (New) The method according to claim 45, wherein said NK1 antagonist is MK-0869 and is administered in a dose ranging between 10 and 160 mg of the active ingredient.

47. (New) The method according to claim 46, wherein MK-0869 is administered in a dose of 80 mg of the active ingredient.

48. (New) The method of claim 26, wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

49. (New) The method of claim 27, wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions,

malinger, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

50. (New) The method of claim 34, wherein said disease or disorder is selected from the group consisting of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.

51. (New) The method of claim 34, wherein said COX-2 inhibitor is chosen from the group consisting of celecoxib, rofecoxib, meloxicam, piroxicam, deracoxib, parecoxib, valdecoxib, etoricoxib, a chromene derivative, a chroman derivative, N-(2-cyclohexyloxynitrophenyl)methane sulfonamide, COX189, ABT963 and JTE-522, or a pro-drug or active metabolite thereof, or a pharmaceutically acceptable salt thereof.

52. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(b) a selective serotonin re-uptake inhibitor,  
as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 6.

53. (New) The pharmaceutical composition according to claim 52 comprising:

(a) pipamperone in a dose ranging between 5 and 15 mg of the active ingredient,  
and

(b) citalopram in a dose ranging between 10 and 40 mg of the active ingredient.

54. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(c) a selective serotonin re-uptake inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 12.

55. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors and

(b) a nor-epinephrine re-uptake inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 12.

56. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a

pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT<sub>2A</sub> receptor with a pKi value equal to or higher than 8 towards the 5-HT<sub>2A</sub> receptor and less than 8 towards other 5HT receptors, and

(c) a nor-epinephrine re-uptake inhibitor,  
as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of the emotional functionality as defined in claim 12.

57. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT<sub>2A</sub> receptor with a pKi value equal to or higher than 8 towards the 5-HT<sub>2A</sub> receptor and less than 8 towards other 5HT receptors, and

(b) a neuroleptic agent,  
as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 12.

58. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT<sub>2A</sub> receptor with a pKi value equal to or higher than 8 towards the 5-HT<sub>2A</sub> receptor and less than 8 towards other



5HT receptors, and

(c) a neuroleptic agent,

as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 12.

59. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(b) an NK1 antagonist,

as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 12.

60. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(c) an NK1 antagonist,

as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined

in claim 12.

61. (New) The pharmaceutical composition according to claim 59 comprising:

(a) pipamperone in a dose ranging between 5 and 15 mg of the active ingredient,  
and

(b) MK-0869 in a dose ranging between 10 and 160 mg of the active ingredient.

62. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(b) a COX-2 inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a musculoskeletal disease or disorder.

63. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(c) a COX-2 inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a musculoskeletal disease or disorder.